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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/428,647	10/28/1999	ROLAND SCHULE	SCH-1700	4945
23599	7590	02/11/2004	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C.			MURPHY, JOSEPH F	
2200 CLARENDON BLVD.			ART UNIT	
SUITE 1400			PAPER NUMBER	
ARLINGTON, VA 22201			1646	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/428,647

Applicant(s)

SCHULE ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 24-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-36 is/are rejected.
- 7) ☒ Claim(s) 1-9 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/29/2003 has been entered.

Formal Matters

Claims 24-36 were added in Paper No. 21, 8/29/2003. Claims 1-9, 24-36 are pending and under consideration.

Specification

The incorporation of essential material in the specification by reference to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). On page 1, lines 1-3 of the instant Specification, Applicant's attempt to incorporate by reference the subject matter of a cited scientific paper (Madgwick et al. (1996) which sets forth the sequence of the SLIM3 protein. However, this document encompasses essential matter, and the sequence of the SLIM3 polypeptide is essential for the practice of a method which makes use of the SLIM3

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polypeptide. Therefore, the above cited document encompasses essential subject matter, which cannot be incorporated by reference to publications (See MPEP 608.01(p)). Clearly, the amino acid sequence of the SLIM3 polypeptide is necessary to practice the claimed method.

Appropriate correction is required.

Claim Objections

Claims 1-9, 24-36 are objected to because of the following informalities: Applicant elected the Group drawn to methods of identifying agents that regulate transcriptional activity of human AR in Paper No. 7, 7/2/2001. The indicated claims contain limitations drawn to non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying agents that regulate the transcriptional activating activity of human AR and human SLIM3, does not reasonably provide enablement for a method of identifying agents that regulate the transcriptional activating activity of biologically active polypeptides with 90%, 95% or 98% sequence identity to human AR and human SLIM3, or a method of identifying agents that regulate the transcriptional activating activity of human AR and modified SLIM3 wherein the SLIM3 polypeptide has 1-10 deletions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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Claims 24-36 encompass methods using biologically active polypeptides with 90%, 95% or 98% sequence identity to human AR and human SLIM3. The claims are thus directed to methods using variant proteins. These claims are overly broad since insufficient guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of SLIM3 or AR. The specification (page 11, line 29 to page 12 line 6) defines SLIM3 derivatives that are determined in that the function according to the examples of the SLIM3 that is described in the literature is compared to the modification. Claims 24-26 and 28-36 do not set forth a functional limitation that the encompassed variant polypeptides must possess. Additionally, claim 27 sets forth the limitation wherein the modified SLIM3 is active in the regulation of transcriptional activation of human AR. However, this function would require that the skilled artisan determine the nature of the activity of SLIM3 in the regulation of AR, then design assays to test for this activity. This would require undue experimentation because Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of human SLIM3 or AR. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle et al. (Mickle JE et al. Genotype-phenotype relationships in cystic fibrosis. *Med Clin North Am.* 2000 May;84(3):597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation,

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delta-F508, a single phenylalanine is deleted at position 508, giving rise to the CF phenotype.

Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (Voet et al. Biochemistry. 1990. John Wiley & Sons, Inc. pages 126-128 and 228-234) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed

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invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make the encompassed polypeptides and practice the claimed method. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polypeptides that the specification only teaches one skilled in the art to test for functional variants. Since the claims do not enable one of skill in the art to make and use the encompassed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for polypeptide variants of human SLIM3 or AR, and has not taught how to make polypeptide variants of SLIM3 or AR, it would require undue experimentation of one of skill in the art to practice a method of identifying agents that regulate the transcriptional activating activity of biologically active polypeptides with 90%, 95% or 98% sequence identity to human AR and human SLIM3, or a method of identifying agents that regulate the transcriptional activating activity of human AR and modified SLIM3 wherein the SLIM3 polypeptide has 1-10 deletions.

Claims 24-36 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

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skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claims 24-36 encompass methods using biologically active polypeptides with 90%, 95% or 98% sequence identity to human AR and human SLIM3. The claims are thus directed to methods using variant proteins, thus these are genus claims. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the human SLIM3 or AR variants. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the genus is insufficiently described. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by

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functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24 and 28 are vague and indefinite in the recitation of the term "biologically active". The term "biologically active" is not defined by the claim, but give no definition of what this activity is. Various biological activities can be attributed to a polypeptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the polypeptide to stimulate antibody production. Claims 25-27, 29-36 are rejected insofar as they depend on the recitation of the term "biologically active".

Conclusion

Claims 1-9 are objected to.

Claims 24-36 are rejected.

Advisory Information

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 571-272-0877.

The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
January 8, 2004